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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/556,356	08/11/2006	Max Peter Seiler	PN/4-33177A	8929

75074 7590 06/19/2008

NOVARTIS INSTITUTES FOR BIOMEDICAL RESEARCH, INC.
400 TECHNOLOGY SQUARE
CAMBRIDGE, MA 02139

EXAMINER	
RAHMANI, NILOOFAR	

ART UNIT	PAPER NUMBER
1625	

MAIL DATE	DELIVERY MODE
06/19/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/556,356	SEILER, MAX PETER	
	Examiner	Art Unit	
	NILOOFAR RAHMANI	1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 August 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5 and 8-14* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3-5 and 8-14* is/are rejected.

7)☒ Claim(s) *2* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *11/10/2005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1-5, and 8-14 are pending in the instant application and claims 6-7 are cancelled.

Priority

2. This application is filed on 08/11/2006, which is a 371 of PCT/EP04/05042, file on 05/11/2004, which claims the priority of UNITED KINGDOM 0310867.7, filed on 05/12/2003.

3. *Claim Rejections - 35 USC § 112*

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 8 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement because the specification does not enable the instant compound to alter the gene expression and therefore to treat any and all known or unknown diseases. The claim contains subject matter, which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue". These factors include 1) the breadth of the claims, 2) the nature of the

invention, 3) the state of the prior art, 4) the level of one of ordinary skill, 5) the level of predictability in the art, 6) the amount of direction provided by the inventor, 7) the existence of working examples, and 8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure. In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

1) The breadth of the claims.
2) The nature of the invention,
3) The state of the prior art,
4) The level of one of ordinary skill,
5) The level of predictability in the art,
6) The amount of direction provided by the inventor,
7) The existence of working examples,
8) The quantity of experimentation needed to make or use the invention based on the content of the disclosure.

The nature of the invention: The instant invention is drawn to method for treatment of psychotic and neurodegenerative disorders, which comprises administering to such subject a therapeutically effective amount of a compound of claim 1.

The state of the prior art: "Patients with dementia with Lewy bodies (DLB) commonly experience psychotic symptoms, most notably visual hallucinations. Previously, it has been shown that visual hallucinations in DLB are assocd. with reduced cortical choline acetyltransferase activity, a marker of cholinergic innervation, but not with predominantly postsynaptic muscarinic M1 receptor binding. In the present investigation, nicotinic acetylcholine receptor (nAChR)

levels in the temporal cortex (Brodmann's areas [BA] 20 and 36) were measured in a group of 24 prospectively assessed DLB patients; comparisons were made between groups with or without visual and auditory hallucinations and delusional misidentification. Visual hallucinations and delusional misidentification were assocd. with lower [125I].alpha.-bungarotoxin binding in areas 36 and 20 (P<.05), but not with changes in [3H]epibatidine binding. There were no significant assocns. with auditory hallucinations. [3H]epibatidine, but not [125I].alpha.-bungarotoxin, binding for all DLB cases was reduced compared to controls (P<.001). Loss of cortical .alpha.7 nicotinic receptors may contribute to hallucinations and delusional misidentification in DLB, with implications for treatment and understanding the mechanisms of psychotic symptoms in dementia." (Court et al., Pharmacology, Biochemistry and Behavior, Vol. 70, 2001, pages 571-579).

The predictability in the art: It is noted that the pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed for physiological activity. *In re Fisher*, 427 F. 2d 833, 166 USPQ 18 (CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute. In the instant case, the instantly claimed invention is highly unpredictable since one skilled in the art would recognize that in regards to the therapeutic effects, whether or not the compounds of formula of claim 1 would be useful for treating a pharmacological condition in a subject.

Amount of guidance/working examples: Applicant provides no guidance for using a therapeutically effective amount of a compound of Formula (I) could treat any and all known or unknown diseases. Nor does applicant identify what diseases are treatable by therapeutically effective amount of a compound of Formula (I).

The breadth of the claims: The breadth of claims is drawn to method for treatment of psychotic and neurodegenerative disorders, which comprises administering to such subject a therapeutically effective amount of a compound of claim 1.

The quantity of undue experimentation needed: Since the guidance and teaching provided by the specification is insufficient for treating diseases associated with therapeutically effective amount of a compound of Formula (I) is efficacious, one of ordinary skill in the art, even with high level of skill, is unable to use the instant compounds as claimed without undue experimentation.

The level of the skill in the art: The level of skill in the art is high. However, due to the unpredictability in the pharmaceutical art, it is noted that each embodiment of the invention is required to be individually assessed for physiological activity by in vitro and in vivo screening to determine which compounds exhibit the desired pharmacological activity and which diseases would benefit from this activity.

Taking all of the above into consideration, it is not seen where the instant claim 8, for treating diseases associated with therapeutically effective amount of a compound of Formula (I) is efficacious, have been enabled by the instant specification.

4. ***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

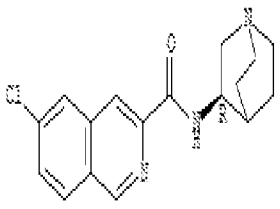
A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1, 3-5, and 8 are rejected under 35 U.S.C. 102(e) as being anticipated by Jacobsen et al., US 7,001,900. Jacobsen et al. disclosed the instant claimed compounds, which from the STN search are

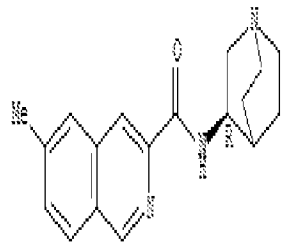
RN 590369-86-1

CN 3-Isoquinolinecarboxamide, N-(3R)-1-azabicyclo[2.2.2]oct-3-yl-6-chloro-



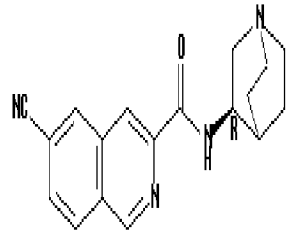
RN 590370-42-6

CN 3-Isoquinolinecarboxamide, N-(3R)-1-azabicyclo[2.2.2]oct-3-yl-6-methyl-



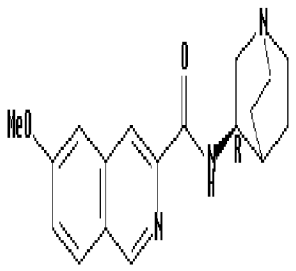
RN 590370-43-7

CN 3-Isoquinolinecarboxamide, N-(3R)-1-azabicyclo[2.2.2]oct-3-yl-6-cyano-



RN 590370-44-8

CN 3-Isoquinolinecarboxamide, N-(3R)-1-azabicyclo[2.2.2]oct-3-yl-6-methoxy-



RN 590370-46-0

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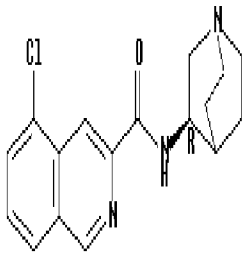
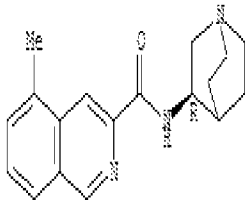


RN 590370-47-1

CN 3-Isoquinolinecarboxamide, N-(3R)-1-azabicyclo[2.2.2]oct-3-yl-5-methyl-

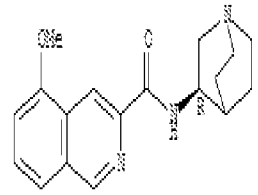


RN 590370-48-2

CN 3-Isoquinolinecarboxamide, N-(3R)-1-azabicyclo[2.2.2]oct-3-yl-5-cyano-

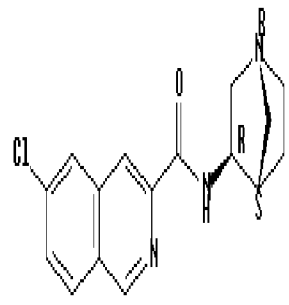
RN 590370-49-3

CN 3-Isoquinolinecarboxamide, N-(3R)-1-azabicyclo[2.2.2]oct-3-yl-5-methoxy-



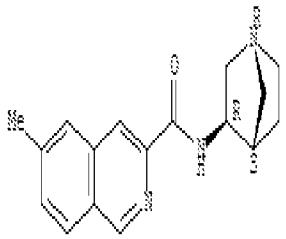
RN 590371-03-2

CN 3-Isoquinolinecarboxamide, N-(1R,3R,4S)-1-azabicyclo[2.2.1]hept-3-yl-6- chloro-



RN 590371-04-3

CN 3-Isoquinolinecarboxamide, N-(1R,3R,4S)-1-azabicyclo[2.2.1]hept-3-yl-6- methyl-



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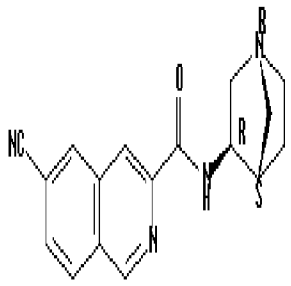
RN 590371-05-4

CN 3-Isoquinolinecarboxamide, N-(1R,3R,4S)-1-azabicyclo[2.2.1]hept-3-yl-6- cyano-



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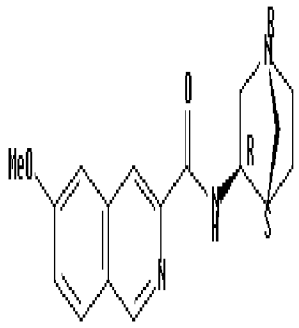
RN 590371-06-5

CN 3-Isoquinolinecarboxamide, N-(1R,3R,4S)-1-azabicyclo[2.2.1]hept-3-yl-6- methoxy-



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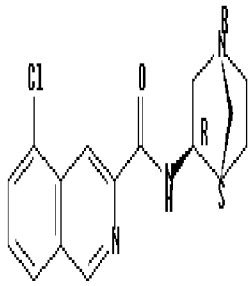
RN 590371-08-7

CN 3-Isoquinolinecarboxamide, N-(1R,3R,4S)-1-azabicyclo[2.2.1]hept-3-yl-5-chloro-



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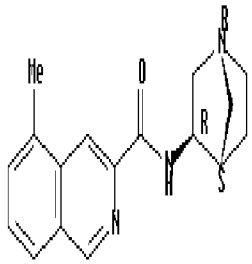
RN 590371-09-8

CN 3-Isoquinolinecarboxamide, N-(1R,3R,4S)-1-azabicyclo[2.2.1]hept-3-yl-5- methyl-



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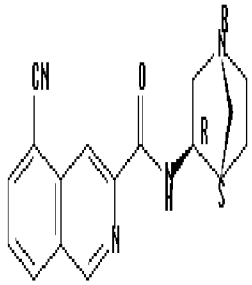
RN 590371-10-1

CN 3-Isoquinolinecarboxamide, N-(1R,3R,4S)-1-azabicyclo[2.2.1]hept-3-yl-5- cyano-



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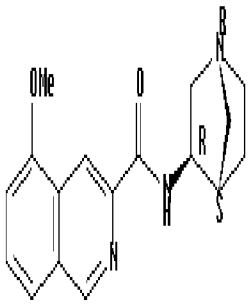
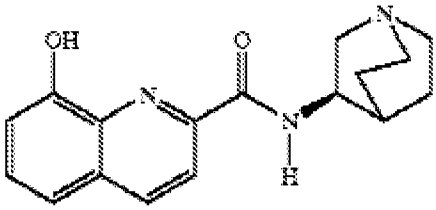
RN 590371-11-2

CN 3-Isoquinolinecarboxamide, N-(1R,3R,4S)-1-azabicyclo[2.2.1]hept-3-yl-5-

methoxy-



, and Example 8, on column 74,

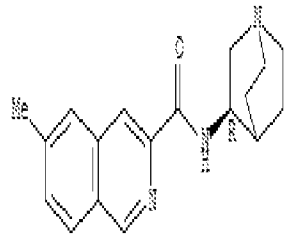


, which these compounds may be in the form of pharmaceutical salts or compositions, may be in pure enantiomeric form of racemic mixtures, and are useful in pharmaceuticals to treat disease or conditions in which α7 is known to be involved. Therefore, the instant claim is anticipated by Jacobsen et al.

5. Claims 1, 3-5, and 8-11 are rejected under 35 U.S.C. 102(e) as being anticipated by Corbett et al., US 2005/0245504. Corbett et al. disclosed the instant claimed compounds, which from the STN search are

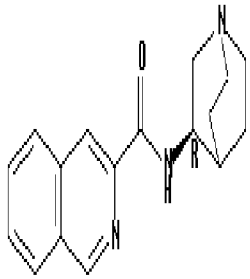
RN 590370-42-6

CN 3-Isoquinolinecarboxamide, N-(3R)-1-azabicyclo[2.2.2]oct-3-yl-6-methyl-



RN 711085-68-6

CN 3-Isoquinolinecarboxamide, N-(3R)-1-azabicyclo[2.2.2]oct-3-yl-

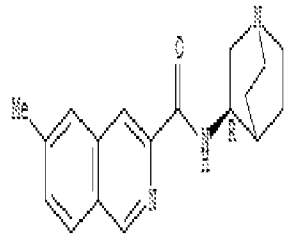


, which these compounds may be in the form of pharmaceutical salts or compositions, may be in pure enantiomeric form of racemic mixtures, and are useful in pharmaceuticals to treat disease or conditions in which α7 is known to be involved. Therefore, the instant claim is anticipated by Corbett et al.

6. Claims 1, 3-5, and 8-11 are rejected under 35 U.S.C. 102(e) as being anticipated by Rogers et al., US 2005/0107425. Rogers et al. disclosed the instant claimed compounds, which from the STN search are

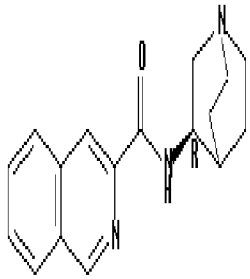
RN 590370-42-6

CN 3-Isoquinolinecarboxamide, N-(3R)-1-azabicyclo[2.2.2]oct-3-yl-6-methyl-



RN 711085-68-6

CN 3-Isoquinolinecarboxamide, N-(3R)-1-azabicyclo[2.2.2]oct-3-yl-

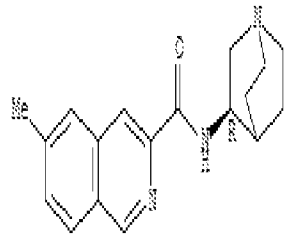


, which these compounds may be in the form of pharmaceutical salts or compositions, may be in pure enantiomeric form of racemic mixtures, and are useful in pharmaceuticals to treat disease or conditions in which α7 is known to be involved. Therefore, the instant claim is anticipated by Rogers et al.

7. Claims 1, 3-5, and 8-11 are rejected under 35 U.S.C. 102(e) as being anticipated by Groppi et al., US 2006/0019984. Groppi et al. disclosed the instant claimed compounds, which from the STN search are

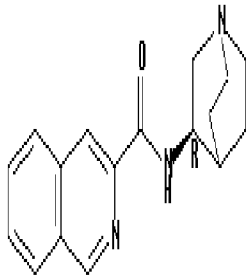
RN 590370-42-6

CN 3-Isoquinolinecarboxamide, N-(3R)-1-azabicyclo[2.2.2]oct-3-yl-6-methyl-



RN 711085-68-6

CN 3-Isoquinolinecarboxamide, N-(3R)-1-azabicyclo[2.2.2]oct-3-yl-



, which these compounds may be in the form of pharmaceutical salts or compositions, may be in pure enantiomeric form of racemic mixtures, and are useful in pharmaceuticals to treat disease or conditions in which α7 is known to be involved. Therefore, the instant claim is anticipated by Groppi et al.

8. ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* ***v.*** *John Deere Co.*, 383 U.S.

1, 148 USPQ 459 (1966), that are applied for establishing a background for

determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 12-14 are rejected under 103(a) as being unpatentable over

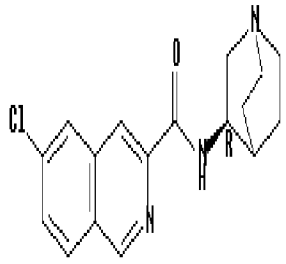
Jacobsen et al., US 7,001,900.

Determination of the scope and content of the prior art (MPEP §2141.01)

Jacobsen et al. disclosed analogous compounds, which form the STN

search are

RN 590369-86-1
CN 3-Isoquinolinecarboxamide, N-(3R)-1-azabicyclo[2.2.2]oct-3-yl-6-chloro-



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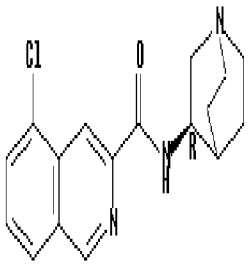
RN 590370-46-0
CN 3-Isoquinolinecarboxamide, N-(3R)-1-azabicyclo[2.2.2]oct-3-yl-5-chloro-



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Ascertainment of the difference between the prior art and the claims (MPEP §2141.02)

The difference between the instant claims and the prior art compound is that the instant claims replace “F” instead of the ”Cl”.

Finding of prima facia obviousness-rational and motivation (MPEP §2142.2143)

One having ordinary skill in the art would be motivated to modify the compounds of Jacobsen et al. to obtain the instant compounds. Because “F” and “Cl" are both halogen. Changing one halogen to another halogen is within skill in the art.

Also note compounds in the prior art, which only differ from the instant compounds in having a different positional isomer for halogen (positions 6 and 8, respectively). Compounds which differ only in the placement of substituents in a ring system is not absent unexpected results. *In re Jones*, 162 F.2d 638, 74 USPQ 152 (CCPA 1947).

9. *Claim Objections*

Claim 2 is objected to as being dependent upon a cancelled base claim 1, but would be allowable if rewritten in independent form including all of the limitations of the base claims and any intervening claims.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Niloofar Rahmani whose telephone number is 571-272-4329. The examiner can normally be reached on Monday through Friday from 8:30 am to 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet Andres, can be reached on 571-272-0867. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/NILOOFAR RAHMANI/

06/09/2008

/D. Margaret Seaman/

Primary Examiner, Art Unit 1625